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(54) Title: **USE OF MALATE DEHYDROGENASE FOR NADH REGENERATION**

(57) Abstract: The present invention relates to a process for the preparation of enantiomerically enriched organic compounds. In particular, the present invention relates to an enzymatically operating process, in which, in a coupled enzymatic reaction system, NAD(P)H is consumed by one enzyme for the preparation of the organic compound and the NAD(P)H is simultaneously regenerated by a second enzyme system. A reaction system which operates according to the invention in this manner and an advantageous whole cell catalyst are also proposed.

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# INTERNATIONAL SEARCH REPORT

International Application No.

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## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12P13/04 C12P7/04 C12P41/00 C12P13/22 C12P13/06  
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According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12P C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, PAJ, EMBASE, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 46363 A (ARISTIDOU ARISTOS ; VALTION TEKNILLINEN (FI); RICHARD PETER (FI); T) 16 September 1999 (1999-09-16) examples 6,7,10,12-15,18,24	1-10
X	US 2002/042110 A1 (MITSUHASHI KAZUYA ET AL) 11 April 2002 (2002-04-11) paragraph '0162!	1-10
X	EP 0 385 415 A (MITSUBISHI PETROCHEMICAL CO) 5 September 1990 (1990-09-05) page 10; example 6	1-8
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE WPI  Section Ch, Week 199001  Derwent Publications Ltd., London, GB;  Class B05, AN 1990-003179  XP002264717  -&amp; JP 01 285193 A (DAICEL CHEM IND LTD),  16 November 1989 (1989-11-16)  page 156  abstract</p>	1-8
X	<p>DATABASE WPI  Section Ch, Week 198630  Derwent Publications Ltd., London, GB;  Class B05, AN 1986-194622  XP002264718  -&amp; JP 61 128895 A (TAKARA SHUZO CO LTD),  16 June 1986 (1986-06-16)  abstract</p>	1-8
X	<p>GU K F ET AL: "PRODUCTION OF ESSENTIAL L  BRANCHED-CHAIN AMINO ACIDS IN BIOREACTORS  CONTAINING ARTIFICIAL CELLS IMMOBILIZED  MULTIENZYME SYSTEMS AND DEXTRAN-NAD"  BIOTECHNOLOGY AND BIOENGINEERING,  vol. 36, no. 3, 1990, pages 263-269,  XP001156578  ISSN: 0006-3592  page 266; figures 2,7</p>	1-8
X	<p>SUYE S: "COENZYME REGENERATION WITH MALIC  ENZYME REACTION SYSTEM"  RECENT RESEARCH DEVELOPMENTS IN  FERMENTATION AND BIOENGINEERING, XX, XX,  vol. 1, no. 1, 1998, pages 55-64,  XP000982890  figure 5; table 1</p>	1-8
X	<p>BOMMARIUS A S ET AL: "BIOCATALYSIS TO  AMINO ACID-BASED CHIRAL  PHARMACEUTICAL-EXAMPLES AND PERSPECTIVES"  JOURNAL OF MOLECULAR CATALYSIS. B,  ENZYMATIC, ELSEVIER, AMSTERDAM,, NL,  vol. 5, 1998, pages 1-11, XP002929513  ISSN: 1381-1177  figure 5</p>	1-8

# INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9946363	A	16-09-1999	FI 980551 A	12-09-1999
			AU 756211 B2	09-01-2003
			AU 2730399 A	27-09-1999
			EP 0981600 A1	01-03-2000
			WO 9946363 A1	16-09-1999
			JP 2001525682 T	11-12-2001
US 2002042110	A1	11-04-2002	JP 2000236883 A	05-09-2000
			EP 1013758 A2	28-06-2000
			US 6312933 B1	06-11-2001
			US 2002127679 A1	12-09-2002
EP 0385415	A	05-09-1990	JP 2227081 A	10-09-1990
			JP 3076581 A	02-04-1991
			DE 69019843 D1	13-07-1995
			EP 0385415 A1	05-09-1990
			US 5416012 A	16-05-1995
			US 5336608 A	09-08-1994
JP 01285193	A	16-11-1989	NONE	
JP 61128895	A	16-06-1986	NONE	